

## Minimizing the risk of occupational Q fever exposure: A protocol for ensuring Coxiella burnetii-negative pregnant ewes are used for medical research.

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### Public Summary:

Q fever is an infectious disease caused by the bacteria *Coxiella burnetii*. Q fever can be transmitted through the air between sheep and human and may persist in the environment for months to years following urine or feces excretion from an infected animal. Symptoms of the disease can range from being asymptomatic, presenting as a flu-like illness, or having severe consequences such as infection of the heart or death. In pregnant women, Q fever has been associated with complications, including premature birth or fetal demise leading to abortion. There is no vaccine for humans commercially available in the USA, so emphasis has been placed on decreasing transmission. This study evaluated the effectiveness of our screening protocol in eliminating Q fever-carrying sheep from our facility in order to protect the safety of our farmers, veterinarians, husbandry staff, laboratory personnel, and abattoir workers who are at a high risk of exposure by working alongside the sheep. Our study consisted of 578 sheep getting tested twice for the Q fever-inducing bacterium, *C. burnetii*. The first test was performed at the vendor prior to breeding the sheep, and the second screen was performed upon the sheep's arrival to the research facility. To test for Q fever, we used a two-phase antibody immunofluorescence assay (IFA) serology. This IFA serology test screens the animal's sample twice to look for two types of antibodies in the sheep's blood, which would indicate that the sheep currently has or was previously exposed to *C. burnetii*. Our results showed 120 of the 844 sheep tested presented with *C. burnetii*. Sheep with two negative Phase I and Phase II IFA results were transported to the research facility. Our second cohort of 272 sheep had 2 sheep test positive after birth. After being quarantined and retested using three additional methods, it was concluded that one of these two sheep tested as a false positive. The other Q fever-positive sheep was euthanized prior to use in a research protocol. No Q fever was reported among husbandry, laboratory or veterinary staff during the study period. In this study, the sensitivity could not be calculated without many cases of Q fever in the sheep population. However, the specificity was 99% when compared to tests on the amniotic fluid. Additionally, although there were possible false-positive results from the IFA serologic testing, more importantly, there were no false-negative IFA serology results identified when compared to the amniotic fluid testing. Therefore, the effectiveness of two negative IFA screening results in our protocol suggests that additional routine testing of the sheep is not necessary. Serologic testing of sheep for the Q fever-inducing bacterium, *C. burnetii*, with IFA before transport and following arrival at a research facility, in combination with reflex testing of amniotic fluid will help limit potential exposure to research staff. Serologic testing of *C. burnetii* with IFA is simple and accurate, and it can be performed using commercially available products.

### Scientific Abstract:

Q fever is a worldwide zoonosis caused by *Coxiella burnetii* that can lead to abortion, endocarditis, and death in humans. Researchers utilizing parturient domestic ruminants, including sheep, have an increased risk of occupational exposure. This study evaluated the effectiveness of our screening protocol in eliminating *C. burnetii*-positive sheep from our facility. From August 2010 to May 2018, all ewes (N = 306) and select lambs (N = 272; ovis aries) were screened twice for *C. burnetii* utilizing a serum Phase I and Phase II antibody immunofluorescence assay (IFA). The first screen was performed by the vendor prior to breeding, and the second screen was performed on arrival to the research facility. Ewes that were positive on arrival screening were quarantined and retested using repeat IFA serology, enzyme-linked immunosorbent assay, buffy coat polymerase chain reaction (PCR), and amniotic fluid PCR. The overall individual seroprevalence of *C. burnetii* in the flocks tested by the vendor was 14.2%. Ewes with negative Phase I and Phase II IFA results were selected for transport to the research facility. Upon arrival to the facility, two (0.7%) ewes had positive Phase I IFA results. Repeat testing demonstrated seropositivity in one of these two ewes, though amniotic fluid PCR was negative in both. The repeat seropositive ewe was

euthanized prior to use in a research protocol. No Q fever was reported among husbandry, laboratory or veterinary staff during the study period. Serologic testing for *C. burnetii* with IFA prior to transport and following arrival to a research facility limits potential exposure to research staff.

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